control by the glycated hemoglobin levels (HbA1c, measured by immuno-inhibition). Total cholesterol (TC), HDL and LDL cholesterol and triglycerides (Tg) were determined by enzymatic methods. IR was calculated using homeostatic model assessment insulin resistance (HOMA-IR) index.

**Results:** We found the highest levels of oxLDL in group A, being significantly higher than in groups B and C (A: 112.2±22.0, B: 95.9±10.2, C: 83.9±8.8, A vs B p<0.05 and A,B vs C p<0.01 ). We found significantly higher Tg levels in group A compared to group B (A: 3.39 ± 0.4, B: 2.49 ± 0.27 mmol/L, A vs B p<0.01) being significantly higher among diabetics in comparison to nondiabetics (C: 2.12±0.2 mmol/L, A vs C p<0.05). Simultaneously, there was no significant difference in the levels of TC, HDL and LDL between the groups. HbA1c level was higher in group A than in group B (A:7.87±0.23, B:6.92±0.13, C:4.9±0.18%; A vs B p<0.05; A, B vs C p<0.01). Similarly, the HOMA-IR values were higher in group A vs group B, and in both of the groups it was higher than in group C (A:10.4±1.4, B:8.5±1.2, C:7.9±0.7; A vs B p<0.01; B vs C p<0.05). In the groups of diabetic patients increased levels of oxLDL significantly correlated with Tg levels (r=0.628, p<0.01), and HOMA–IR (r=0.399, p<0.05) while oxLDL significantly correlated with HbA1c only in group A (r=0.697; p<0.001), but not in groups B and C (p=NS).

**Conclusion:** Our results have demonstrated that in patients with T2D and CAD increased oxLDL levels could be good residual lipid risk marker. Atherogenic potential in T2D is associated predominantly with the increased oxLDL, higher IR and impairments in triglycerides metabolism but not with the levels of lipoproteins. Also, the results imply that in T2D patients LDL oxidation is significantly influenced by the impairments in glucose control.

**OP4: Metformin decreases plasma levels of fibulin-1, a novel marker of arterial matrix alterations in diabetes**

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**Background and aims:** We recently identified fibulin-1-mRNA as the most upregulated transcript in non-atherosclerotic arterial tissue from patients with type 2 diabetes. Fibulin-1 is an elastin- and basement membrane-associated extracellular matrix protein also present in plasma. In addition, we observed higher amounts of fibulin-1-protein in the arterial wall and in the circulation among patients with diabetes. Moreover, we showed an association between increased levels of plasma fibulin-1 and arterial stiffness and demonstrated independent mortality-predictive abilities of plasma fibulin-1 in type 2 diabetes. These published results suggest that fibulin-1 is involved in the development of arterial disease in type 2 diabetes and that the circulating levels may serve as a biomarker for diabetic arteriopathy.

Metformin is an anti-diabetic drug with documented beneficial CVD effects in diabetes. The explanation may include direct, but unknown, effects of metformin on the arterial wall. We hypothesized that metformin would influence the increased level of plasma fibulin-1 in diabetics.

**Materials and Methods:** The study is an investigator driven, prospective, randomized, and partly placebo controlled trial with 450 type 2 diabetic patients. After a four week run-in period, 371 eligible patients were randomized to one of eight treatment groups in a factorial design with NPH insulin vs. insulin aspart, metformin vs. placebo, or rosiglitazone vs. placebo. Plasma fibulin-1 was analyzed by an ELISA (in house, previously described) and HbA1c by HPLC (TOSOH) at the beginning of the study and after 18 and 24 months.

**Results:** Plasma fibulin-1 increased in all groups throughout the two-year period; however, the increase was strongly reduced among patients treated with metformin. A highly significant difference was observed, when the mean change in plasma fibulin-1 was compared between metformin and not-metformin treated individuals both at 18 and 24 months of treatment (p<0.001). No such difference was seen when the rosiglitazone treated group was compared to the non-rosiglitazone treated group. Both metformin and rosiglitazone reduced the HbA1c levels to comparable levels. There was no correlation between changes in plasma fibulin-1 and changes in HbA1c.

**Conclusion:** Metformin treatment reduces plasma fibulin-1 concentrations among patients with type 2 diabetes, an effect which is independent of glycemic effects. Changes in fibulin-1 may reflect an important element in diabetic arteriopathy, which can be influenced by metformin.

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